

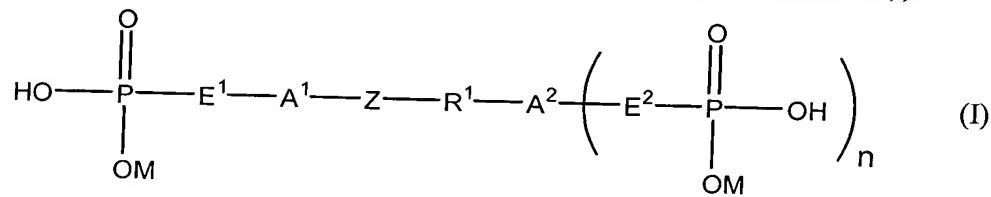
is attached hereto in an addendum entitled "ADDENDUM TO PRELIMINARY AMENDMENT DATED APRIL 8, 2002". In this addendum, changes are indicated by underlining added text and by striking out deleted text.

In the Claims:

Cancel claims 1-20.

Add new claims 21-77, as follows:

21. A method for inhibiting activity of an alkaline phosphatase, said method comprising contacting the alkaline phosphatase with a compound of formula (I):



where:

A¹ and A² are the same or different aryl groups collectively bearing at least one hydrophilic substituent;

E¹ and E² are the same or different and are O, S, or NR² (where R² is H or a linear or branched C₁-C₂₀ carbon containing group);

M is H or a pharmaceutically acceptable monovalent cation;

R¹ is a linear or branched, saturated or unsaturated, C₁-C₂₀ carbon containing group;

Z is a single bond, a carbonyl, CE³E⁴, or CR³E⁴, where

E³ and E⁴ are the same or different and are OR⁴, SR⁴, and NR₂R⁴, where

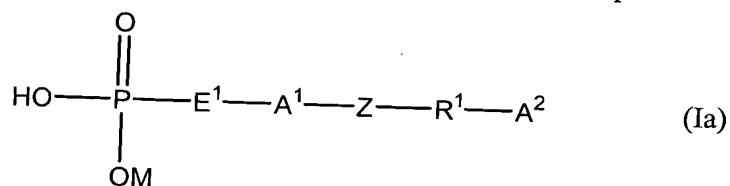
R³ is a linear or branched C₁-C₂₀ carbon containing group, and

R⁴ is H or a linear or branched C₁-C₂₀ carbon containing group; and

n is 0 or 1,

or a pharmaceutically acceptable salt thereof under conditions effective to inhibit the alkaline phosphatase's activity.

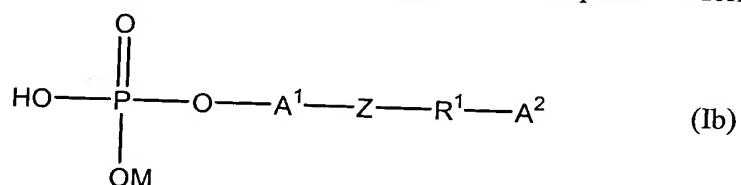
22. The method of claim 21 where the compound is a compound of formula (Ia):



where:

A^1 , A^2 , E^1 , M , R^1 and Z are as defined in claim 21, or a pharmaceutically acceptable salt thereof.

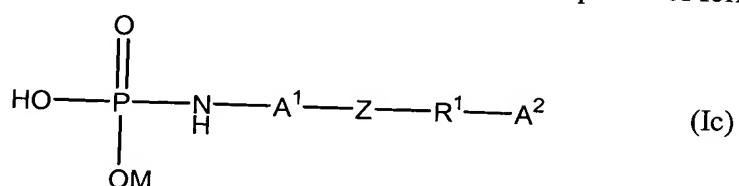
23. The method of claim 21 where the compound is a compound of formula (Ib):



where:

A^1 , A^2 , E^1 , M , R^1 and Z are as defined in claim 21, or a pharmaceutically acceptable salt thereof.

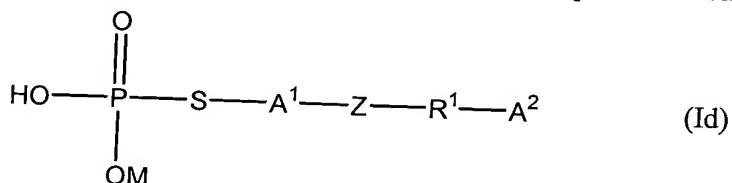
24. The method of claim 21 where the compound is a compound of formula (Ic):



where:

A^1, A^2, M, R^1 and Z are as defined in claim 21, or a pharmaceutically acceptable salt thereof.

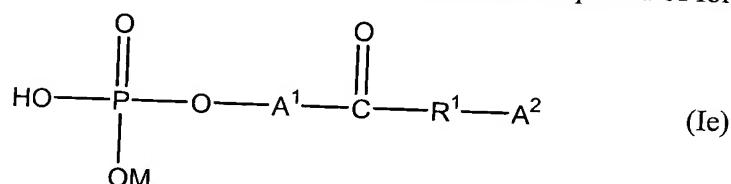
25. The method of claim 21 where the compound is a compound of formula (Id):



where:

A^1, A^2, M, R^1 and Z are as defined in claim 21, or a pharmaceutically acceptable salt thereof.

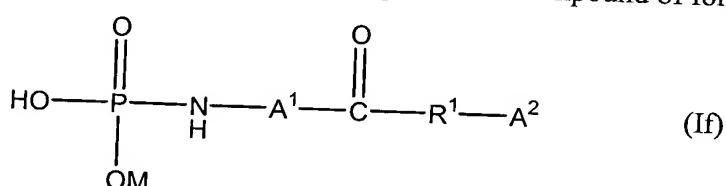
26. The method of claim 21 where the compound is a compound of formula (Ie):



where:

A^1, A^2, M , and R^1 are as defined in claim 21, or a pharmaceutically acceptable salt thereof.

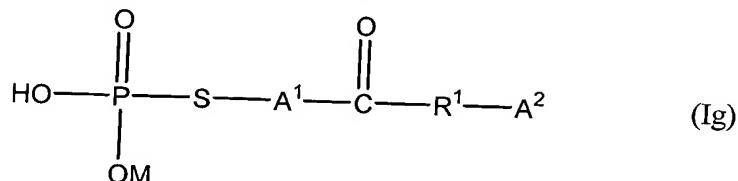
27. The method of claim 21 where the compound is a compound of formula (If):



where:

A^1, A^2, M , and R^1 are as defined in claim 21, or a pharmaceutically acceptable salt thereof.

28. The method of claim 21 where the compound is a compound of formula (Ig):



where:

A^1 , A^2 , M , and R^1 are as defined in claim 21, or a pharmaceutically acceptable salt thereof.

29. The method of claim 21 where the compound is a compound is 2'-phosphophloretin, 2'-thiophosphophloretin, 2'-aminophosphophloretin, 3-azido-2'-phosphophloretin, or 4-azido-2'-phosphophloretin or a pharmaceutically acceptable salt thereof

30. The method of claim 21, wherein the compound is not 4'-phosphophloretin or a pharmaceutically acceptable salt thereof.

31. The method of claim 21, wherein, when E^1 is O and when Z is a carbonyl and when A^1 is a phenyl ring and when E^1 is at the 2-position of the phenyl ring A^1 and when the phenyl ring A^1 is further substituted in the 4- and 6- positions thereof with OR^5 groups (where R^5 is a carbon containing group having between 1 and 4 carbon atoms), A^2 is not a phenyl ring substituted in the 4-position thereof with an OR^5 group (where R^5 is a carbon containing group having between 1 and 4 carbon atoms).

32. The method of claim 31, wherein, when E¹ is O and when Z is a carbonyl and when A¹ is a phenyl ring and when E¹ is at the 2-position of the phenyl ring A¹, A¹ is not further substituted in the 4- and 6-positions of the phenyl ring A¹ with OR⁵ groups (where R⁵ is a carbon containing group having between 1 and 4 carbon atoms).

33. The method of claim 21, wherein E¹ is O and wherein A² is a phenyl ring bearing an OH group in the 4-position thereof.

34. The method of claim 21, wherein E¹ is O; wherein A¹ is a phenyl ring; wherein E¹ is at the 2-position of the phenyl ring A¹; and wherein the phenyl ring A¹ is further substituted with an OH group in the 4-position thereof.

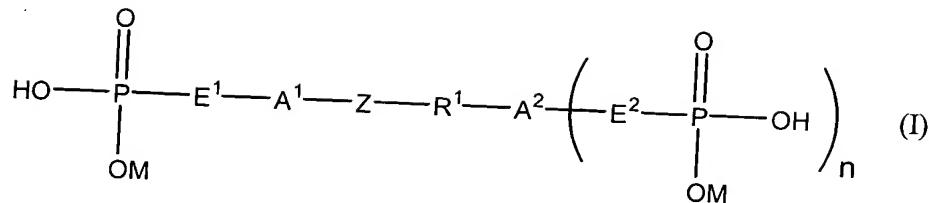
35. The method of claim 21, wherein E¹ is O and wherein A¹ is a phenyl ring; wherein E¹ is at the 2-position of the phenyl ring A¹; and wherein the phenyl ring A¹ is further substituted with an OH group in the 6-position thereof.

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36. The method of claim 21, wherein E¹ is O and wherein A¹ is a phenyl ring; wherein E¹ is at the 2-position of the phenyl ring A¹; and wherein the phenyl ring A¹ is further substituted with OH groups in the 4- and 6-positions thereof.

37. The method of claim 21, wherein E¹ is O; wherein A² is a phenyl ring bearing an OH group in the 4-position thereof; wherein A¹ is a phenyl ring; wherein E¹ is at the 2-position of the phenyl ring A¹; and wherein the phenyl ring A¹ is further substituted with OH groups in the 4- and 6-positions thereof.

38. The method of claim 21, wherein A¹ is a phenyl ring and E¹ is at the 2-position of the phenyl ring A¹.

39. A method for inhibiting activity of an alkaline phosphatase in a subject, said method comprising administering to the subject a compound of formula (I):



where:

A^1 and A^2 are the same or different aryl groups collectively bearing at least one hydrophilic substituent;

E^1 and E^2 are the same or different and are O, S, or NR^2 (where R^2 is H or a linear or branched C_1 - C_{20} carbon containing group);

M is H or a pharmaceutically acceptable monovalent cation;

R^1 is a linear or branched, saturated or unsaturated, C_1 - C_{20} carbon containing group;

Z is a single bond, a carbonyl, CE^3E^4 , or CR^3E^4 , where

E^3 and E^4 are the same or different and are OR^4 , SR^4 , and NR^4_2 , where

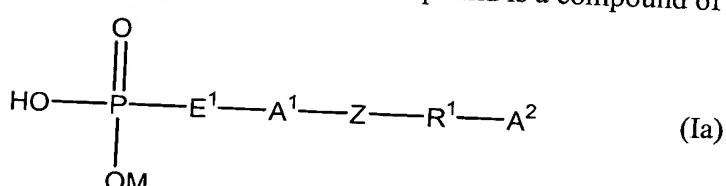
R^3 is a linear or branched C_1 - C_{20} carbon containing group, and

R^4 is H or a linear or branched C_1 - C_{20} carbon containing group; and

n is 0 or 1,

or a pharmaceutically acceptable salt thereof.

40. The method of claim 39 where the compound is a compound of formula (Ia):

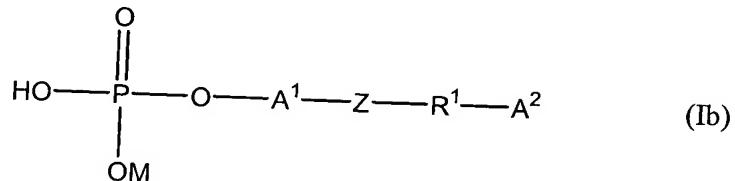


where:

A^1 , A^2 , E^1 , M , R^1 and Z are as defined in claim 21, or a pharmaceutically acceptable salt thereof.

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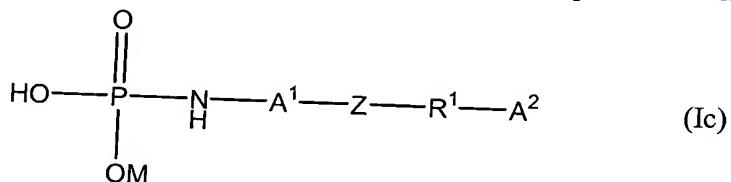
41. The method of claim 39 where the compound is a compound of formula (Ib):



where:

A^1 , A^2 , E^1 , M , R^1 and Z are as defined in claim 39, or a pharmaceutically acceptable salt thereof.

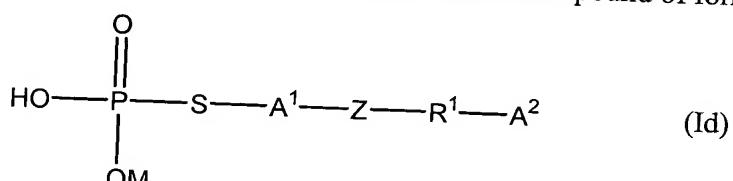
42. The method of claim 39 where the compound is a compound of formula (Ic):



where:

A^1 , A^2 , M , R^1 and Z are as defined in claim 39, or a pharmaceutically acceptable salt thereof.

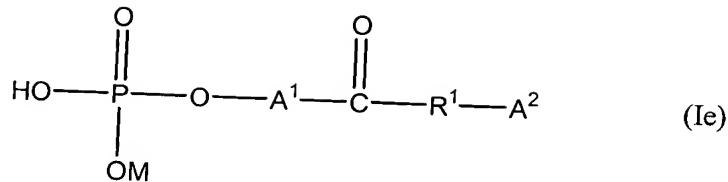
43. The method of claim 39 where the compound is a compound of formula (Id):



where:

A^1 , A^2 , M , R^1 and Z are as defined in claim 39, or a pharmaceutically acceptable salt thereof.

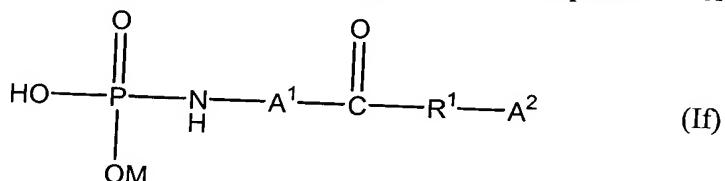
44. The method of claim 39 where the compound is a compound of formula (Ie):



where:

A^1 , A^2 , M , and R^1 are as defined in claim 39, or a pharmaceutically acceptable salt thereof.

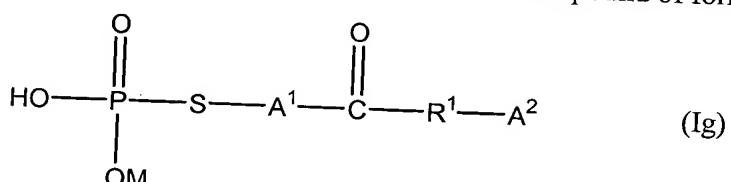
45. The method of claim 39 where the compound is a compound of formula (If):



where:

A^1 , A^2 , M , and R^1 are as defined in claim 39, or a pharmaceutically acceptable salt thereof.

46. The method of claim 39 where the compound is a compound of formula (Ig):



where:

A^1 , A^2 , M , and R^1 are as defined in claim 39, or a pharmaceutically acceptable salt thereof.

47. The method of claim 39 where the compound is a compound of 2'-phosphophloretin, 2'-thiophosphophloretin, 2'-aminophosphophloretin, 3-azido-2'-

phosphophloretin, or 4-azido-2'-phosphophloretin or a pharmaceutically acceptable salt thereof.

48. The method of claim 39, wherein the compound is not 4'-phosphophloretin or a pharmaceutically acceptable salt thereof.

49. The method of claim 39, wherein, when E^1 is O and when Z is a carbonyl and when A^1 is a phenyl ring and when E^1 is at the 2-position of the phenyl ring A^1 and when the phenyl ring A^1 is further substituted in the 4- and 6- positions thereof with OR^5 groups (where R^5 is a carbon containing group having between 1 and 4 carbon atoms), A^2 is not a phenyl ring substituted in the 4-position thereof with an OR^5 group (where R^5 is a carbon containing group having between 1 and 4 carbon atoms).

50. The method of claim 49, wherein, when E^1 is O and when Z is a carbonyl and when A^1 is a phenyl ring and when E^1 is at the 2-position of the phenyl ring A^1 , A^1 is not further substituted in the 4- and 6-positions of the phenyl ring A^1 with OR^5 groups (where R^5 is a carbon containing group having between 1 and 4 carbon atoms).

51. The method of claim 39, wherein E^1 is O and wherein A^2 is a phenyl ring bearing an OH group in the 4-position thereof.

52. The method of claim 39, wherein E^1 is O; wherein A^1 is a phenyl ring; wherein E^1 is at the 2-position of the phenyl ring A^1 ; and wherein the phenyl ring A^1 is further substituted with an OH group in the 4-position thereof.

53. The method of claim 39, wherein E^1 is O and wherein A^1 is a phenyl ring; wherein E^1 is at the 2-position of the phenyl ring A^1 ; and wherein the phenyl ring A^1 is further substituted with an OH group in the 6-position thereof.

54. The method of claim 39, wherein E^1 is O and wherein A^1 is a phenyl ring; wherein E^1 is at the 2-position of the phenyl ring A^1 ; and wherein the phenyl ring A^1 is further substituted with OH groups in the 4- and 6-positions thereof.

55. The method of claim 39, wherein E^1 is O; wherein A^2 is a phenyl ring bearing an OH group in the 4-position thereof; wherein A^1 is a phenyl ring; wherein E^1 is at the 2-position of the phenyl ring A^1 ; and wherein the phenyl ring A^1 is further substituted with OH groups in the 4- and 6-positions thereof.

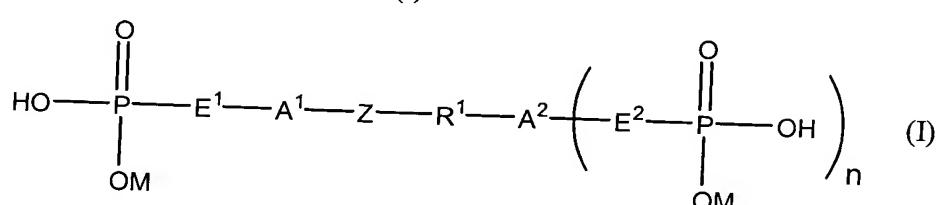
56. The method of claim 39, wherein A^1 is a phenyl ring and E^1 is at the 2-position of the phenyl ring A^1 .

57. The method of claim 39, where the administration is intermittent.

58. The method of claim 39, where the administration is oral.

59. The method of claim 39, where the administration is parenteral.

60. A method for inhibiting sodium-mediated phosphate uptake, said method comprising contacting a compound of formula (I):



where:

A^1 and A^2 are the same or different aryl groups collectively bearing at least one hydrophilic substituent;

E^1 and E^2 are the same or different and are O, S, or NR^2 (where R^2 is H or a linear or branched C_1 - C_{20} carbon containing group);

M is H or a pharmaceutically acceptable monovalent cation;

R^1 is a linear or branched, saturated or unsaturated, C_1 - C_{20} carbon containing group;

Z is a single bond, a carbonyl, CE^3E^4 , or CR^3E^4 , where

E^3 and E^4 are the same or different and are OR^4 , SR^4 , and NR^4_2 , where

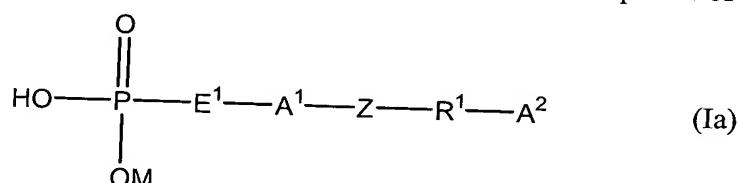
R^3 is a linear or branched C_1 - C_{20} carbon containing group, and

R^4 is H or a linear or branched C_1 - C_{20} carbon containing group; and

n is 0 or 1,

or a pharmaceutically acceptable salt thereof, with intestinal brush border membrane under conditions effective to inhibit sodium-mediated phosphate uptake.

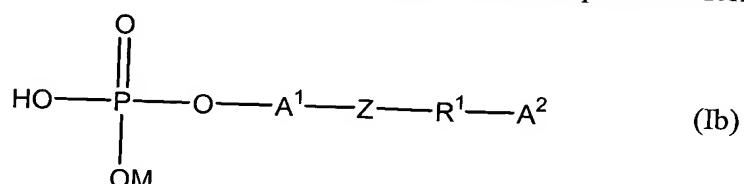
61. The method of claim 60 where the compound is a compound of formula (Ia):



where:

A^1 , A^2 , E^1 , M, R^1 and Z are as defined in claim 60, or a pharmaceutically acceptable salt thereof.

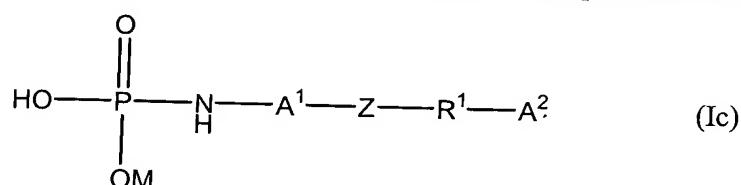
62. The method of claim 60 where the compound is a compound of formula (Ib):



where:

A^1 , A^2 , E^1 , M , R^1 and Z are as defined in claim 60, or a pharmaceutically acceptable salt thereof.

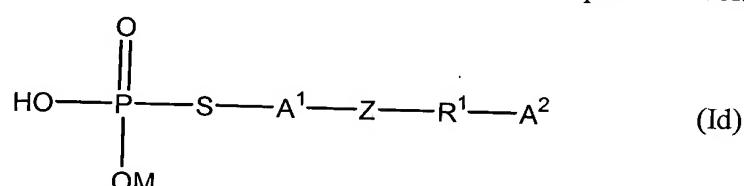
63. The method of claim 60 where the compound is a compound of formula (Ic):



where:

A^1 , A^2 , M , R^1 and Z are as defined in claim 60, or a pharmaceutically acceptable salt thereof.

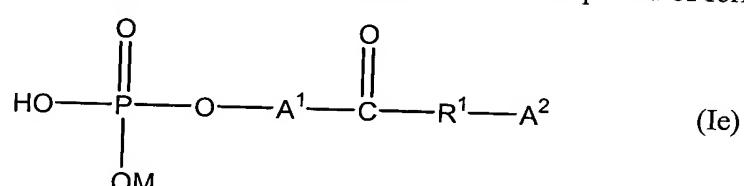
64. The method of claim 60 where the compound is a compound of formula (Id):



where:

A^1 , A^2 , M , R^1 and Z are as defined in claim 60, or a pharmaceutically acceptable salt thereof.

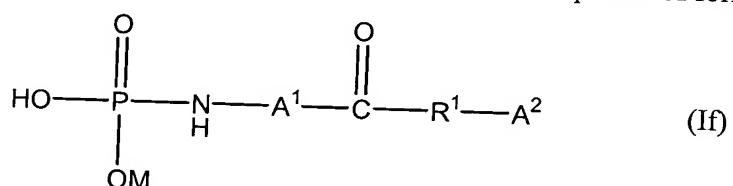
65. The method of claim 60 where the compound is a compound of formula (Ie):



where:

A^1 , A^2 , M , and R^1 are as defined in claim 60, or a pharmaceutically acceptable salt thereof.

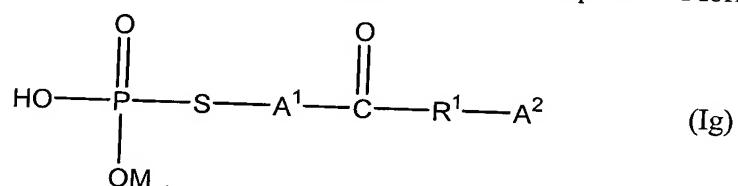
66. The method of claim 60 where the compound is a compound of formula (If):



where:

A^1 , A^2 , M , and R^1 are as defined in claim 60, or a pharmaceutically acceptable salt thereof.

67. The method of claim 60 where the compound is a compound of formula (Ig):



where:

A^1 , A^2 , M , and R^1 are as defined in claim 60, or a pharmaceutically acceptable salt thereof.

68. The method of claim 60 where the compound is 2'-phosphophloretin, 2'-thiophosphophloretin, 2'-aminophosphophloretin, 3-azido-2'-phosphophloretin, or 4-azido-2'-phosphophloretin or a pharmaceutically acceptable salt thereof.

69. The method of claim 60, wherein the compound is not 4'-phosphophloretin or a pharmaceutically acceptable salt thereof.

70. The method of claim 60, wherein, when E^1 is O and when Z is a carbonyl and when A^1 is a phenyl ring and when E^1 is at the 2-position of the phenyl ring A^1 and when the phenyl ring A^1 is further substituted in the 4- and 6- positions thereof with OR^5 groups (where R^5 is a carbon containing group having between 1 and 4 carbon atoms), A^2 is not a phenyl ring substituted in the 4-position thereof with an OR^5 group (where R^5 is a carbon containing group having between 1 and 4 carbon atoms).

71. The method of claim 70, wherein, when E^1 is O and when Z is a carbonyl and when A^1 is a phenyl ring and when E^1 is at the 2-position of the phenyl ring A^1 , A^1 is not further substituted in the 4- and 6-positions of the phenyl ring A^1 with OR^5 groups (where R^5 is a carbon containing group having between 1 and 4 carbon atoms).

72. The method of claim 60, wherein E^1 is O and wherein A^2 is a phenyl ring bearing an OH group in the 4-position thereof.

73. The method of claim 60, wherein E^1 is O; wherein A^1 is a phenyl ring; wherein E^1 is at the 2-position of the phenyl ring A^1 ; and wherein the phenyl ring A^1 is further substituted with an OH group in the 4-position thereof.

74. The method of claim 60, wherein E^1 is O and wherein A^1 is a phenyl ring; wherein E^1 is at the 2-position of the phenyl ring A^1 ; and wherein the phenyl ring A^1 is further substituted with an OH group in the 6-position thereof.

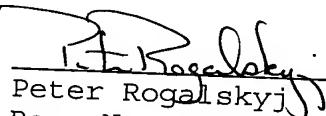
75. The method of claim 60, wherein E^1 is O and wherein A^1 is a phenyl ring; wherein E^1 is at the 2-position of the phenyl ring A^1 ; and wherein the phenyl ring A^1 is further substituted with OH groups in the 4- and 6-positions thereof.

76. The method of claim 60, wherein E¹ is O; wherein A² is a phenyl ring bearing an OH group in the 4-position thereof; wherein A¹ is a phenyl ring; wherein E¹ is at the 2-position of the phenyl ring A¹; and wherein the phenyl ring A¹ is further substituted with OH groups in the 4- and 6-positions thereof.

77. The method of claim 60, wherein A¹ is a phenyl ring and E¹ is at the 2-position of the phenyl ring A¹.

Respectfully submitted,

April 8, 2002
Date

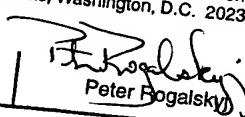

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4-8-02
Date


Peter Rogalsky